## Scientific Abstract

Central to the realization of the potential of gene therapy for malignancy is the ability to accomplish efficient and specific gene delivery to cancer cells. To this end, the Gene Therapy Program at UAB has developed a major focus in the area of vector improvement. Specifically, we have shown that our "tropism-modified" adenoviral vectors accomplish dramatically enhanced gene transfer to human tumor cells when compared to adenoviral vectors traditionally employed. It is our hypothesis that modifications of adenoviral vectors to increase their specificity and efficiency will allow enhanced tumor cell transduction, and by virtue of this achievement, an enhanced therapeutic effect in the context of a cancer gene therapy approach for carcinoma of the ovary. Accordingly, pursuant to validating the hypothesis, this research proposal includes a human gene therapy protocol for ovarian and extraovarian cancer patients with persistent or recurrent disease. This Phase I protocol will 1) determine the maximally tolerated dose and spectrum of toxicities encountered with intraperitoneal delivery of an antibody fragment (Fab') modified, fibroblast growth factor (FGF2) enhanced adenovirus encoding Herpes Simplex Virus thymidine kinase (HSV-TK) given in combination with intravenous ganciclovir (GCV) in previously treated ovarian and extraovarian patients, 2)determine the safety of administration of intraperitoneally delivered FGF2-Fab' modified adenovirus encoding HSV-TK given in combination with intravenous GCV in previously treated ovarian/extraovarian cancer patients, 3)determine gene transfer efficiency of intraperitoneally administered FGF2-Fab' modified recombinant adenovirus, and 4)determine the ability of intraperitoneally delivered FGF2-Fab' modified adenovirus encoding HSV-TK to modify the host immune response. This novel vector strategy has been highly promising in *in vitro* and *in vivo* studies. It is anticipated that the experiments described herein would establish the safety and provide an indication of efficacy of this approach in human subjects with ovarian cancer and allow the rapid evaluation of the clinical utility of this novel therapeutic in future Phase II/III trials.